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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,495	04/13/2006	Gabriella Sozzi	0471-0291PUS1	7078

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
08/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/538,495	SOZZI, GABRIELLA	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The finality as set forth in the Office action mailed 4/2/09 is withdrawn. The response filed 7/29/09 has been entered. Claims 1, 3-4 and 6-11 are pending.

1. Applicant's arguments with respect to claims 1, 3-4, and 6-11 have been considered but are moot in view of the new ground(s) of rejection.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 3-4, 7-8 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678) in view of Chang et al. (6,664,046, issued Dec. 16, 2003) and Cook (7,160,996, issued Jan. 9, 2007).

Sozzi et al. disclose circulating DNA quantification with plasma DNA in 84 patients with non-small cell lung cancer (see 4675, the Abstract). The sample is a DNA sample (see pg. 4675, column 2, forth-fifth paragraph). Polymerase chain reaction is performed for quantification (see 4676, column 1, forth paragraph). The data suggest that quantification of plasma DNA in lung cancer patients is a valuable noninvasive diagnostic tool for discriminating from unaffected individuals and for detecting early recurrence during follow-up (See pg. 4675, the Abstract). The circulating plasma DNA is compared with controls (see pg. 4676, table1).

Sozzi et al. do not disclose steps 2)-5).

Chang et al. disclose a method of quantitation of expression of hTERT mRNA (See column 2, lines 1-3). The level of hTERT mRNA expression assists in the diagnosis of cancers (See column 2, lines 9-10). The method involves amplifying a target hTERT mRNA sequence using a pair of primers (See column 2, lines 46-47) in which the target RNA is amplified by first reverse transcribing and then amplifying the resulting cDNA (see column 8, lines 49-59). The amplification is carried out using a DNA polymerase with 5' to 3' exonuclease activity. The amplified hTERT mRNA sequence is detected by probe hybridization (See column 2, lines 59-62). The detection probe is labeled with two fluorescent dyes, one of which is capable of quenching the fluorescence of the other dye. One dye is attached to the 5' end and the other is attached to an internal site (See column 9, lines 47-55, and column 19, lines 9-15). Quantitation of a sample containing an unknown number of target sequences typically is carried out with reference to a "standard curve" generated from a series of amplifications of samples containing the target sequence in a range of known amounts (See column 10, lines 14-18).

Actually, the method of quantitation of hTERT mRNA as taught by Chang et al. is based upon the sample copy number which is measuring the increase in amplified nucleic acid by monitoring the increase in the total amount of double-standard DNA in the reaction mixture (see column 9, lines 65-67 to column 10, lines 10-13). The instant claims require that the concentration of circulating total DNA in a plasma sample be determined by quantifying the hTERT DNA copy number. Thus the teachings of Chang et al. satisfy the limitations of instant claim 1 as recited in steps 2)-5).

One of ordinary skill in the art would have been motivated to add a mixture of oligonucleotide primers suitable for PCR amplification of a fragment of an hTERT gene because

Chang et al. disclose that the level of hTERT mRNA expression assists in the diagnosis of cancers (See column 2, lines 9-10) and Chang et al. disclose a method of quantifying hTERT mRNA via quantifying cDNA. It would have been prima facie obvious to apply a primer which is for amplifying a fragment of an hTERT gene.

Chang et al. do not disclose one quencher or one reporter fluorophore located at the 3' end.

Cook discloses a new class of fluorescence energy transfer probes with optimized characteristics for genetic detection, discrimination and quantitation (See column 3, lines 43-45) in which a quencher is located at the 3' end of the probe (See fig. 5).

One of ordinary skill in the art would have been motivated to apply the probe of Cook in the method of Chang et al. for the quantitation of expression of hTERT mRNA because the probes of Cook possess optimized characteristics for genetic detection, discrimination and quantitation (See column 3, lines 43-45). It would have been prima facie obvious to use a probe which has a quencher located at the 3' end of the probe.

None of references above discloses the reference concentration as recited in claim 4.

However, one of ordinary skill in the art would have been motivated to optimize the reference concentration with a reasonable expectation of success because optimization of reaction conditions was a routine practice in the art at the time the invention was made (see M.P.E.P. 2144.05). It would have been prima facie obvious to apply a reference concentration as recited in claim 4.

4. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678) in view of Chang et al. (6,664,046,

issued Dec. 16, 2003) and Cook (7,160,996, issued Jan. 9, 2007) as applied to claims 1, 3-4, 7-8 and 10-11 above, and further in view of Wick et al. (Gene, 1999, Vol. 232, pg. 97-106), Lowe et al. (Nucleic Acids Research, 1990, Vol. 18(7), pg. 1757-1761) and the attached search report.

The teachings of Sozzi et al, Chang et al., and Cook are set forth in section 3 above. None of the references discloses SEQ ID NO: 1-3 used as primers and a probe for amplifying the fragment of hTERT gene.

Wick et al. disclose the complete genomic organization of the hTERT gene and isolated the 5'- and 3' flanking region. The hTERT gene encompasses more than 37kb and consists of 16 exons. These results provide the basis for more detailed studies on the regulation of telomerase activity in normal and cancer cells and may lead to the development of new cancer therapies (See pg. 97, the Abstract). As indicated in the search report, the nucleic acid sequence of the hTERT gene comprises SEQ ID NO: 1-3 (See the attached search report).

Lowe et al. disclose criteria for primer selection from known nucleotide sequences (see pg. 1758, column 1).

One of ordinary skill in the art would have been motivated to design primers and probes from a known nucleic acid sequence, for example, the nucleic acid of hTERT gene as disclosed by Wick et al. for amplifying the fragment of the hTERT because Lowe et al. disclose criteria for primer selection (see pg. 1758, column 1). It would have been prima facie obvious to use SEQ ID NO: 1-3 as primers and probes for amplifying a fragment of hTERT gene.

5. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sozzi et al. (Cancer Research, June 15, 2001, Vol. 61, pg. 4675-4678), in view of Chang et al. (6,664,046,

issued Dec. 16, 2003) and Cook (7,160,996, issued Jan. 9, 2007) and as applied to claims 1, 3-4, 7-8 and 10-11 above, and further in view of Gocke et al. (6,156,504 issued Dec. 5, 2000).

The teachings of Sozzi et al., Chang et al., and Cook are set forth in section 3 above. None of the references discloses the limitation of claim 9.

Gocke et al. disclose methods for detecting the presence of extracellular DNA in blood plasma via DNA amplification for the detection, monitoring or evaluation of cancer or premalignant conditions (See column 3, lines 66-67 and column 4, lines 1-7). The method provides for screening both healthy individuals, and individuals at risk for cancer and premalignant conditions (See column 8, lines 59-61) including lung cancer from smokers (See column 30, lines 63-67).

One of ordinary skill in the art would have been motivated to apply the method of Sozzi et al. for the evaluation of the risk of cancer development in smokers because the method of Gocke et al. discloses detecting the presence of extracellular DNA in blood plasma via DNA amplification for the detection, monitoring or evaluation of cancer or premalignant conditions (See column 3, lines 66-67 and column 4, lines 1-7) including lung cancer from smokers (See column 30, lines 63-67). It would have been prima facie obvious to carry out evaluation of the risk of cancer development in smokers as claimed.

Summary

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
August 9, 2009